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| 09/844,662      | 04/27/2001  | Eva Raschke          | 8325-0012           | 9004             |

20855 7590 09/23/2005

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| EXAMINER |
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WAX, ROBERT A

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| ART UNIT | PAPER NUMBER |
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1653

DATE MAILED: 09/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/844,662

Applicant(s)

RASCHKE ET AL.

Examiner

Robert A. Wax

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 08 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-3, 6-18, 20-24, 27 and 57-86 is/are pending in the application.
- 4a) Of the above claim(s) 1-3, 6-18, 20-24, 27, 58, 59, 61 and 72-86 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 57, 60, 62-68, 70 and 71 is/are rejected.
- 7) ☒ Claim(s) 69 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

**DETAILED ACTION**

***Claim Rejections - 35 USC § 102***

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 57, 62-68, 70 and 71 are again rejected under 35 U.S.C. 102(e) as being clearly anticipated by Cox, III et al.

Cox, III et al., in Example VI, "demonstrate that a designed ZFP can repress expression of an endogenous cellular gene that is in its natural context and chromatin structure. Specifically, effector plasmids expressing VEGF ZFPs fused to the KRAB repression domain were introduced into cells and were shown to down-regulate the VEGF gene." See column 51, lines 40-45. The fact that they down-regulated the VEGF gene means that the ZFPs were bound to the DNA and formed the complex claimed in the instant claims. Thus, the above claims are clearly anticipated.

3. Claim 60 is rejected under 35 U.S.C. 102(e) as being clearly anticipated by Cox, III et al. as evidenced by Neely et al.

The teachings of Cox, III et al. are outlined above.

Neely et al. teach that zinc finger 4 of Transcription Factor IIIA binds in the minor groove.

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It is considered that, while all zinc finger proteins are not the same, all of them do have multiple zinc finger domains and it seems reasonable to conclude that other zinc finger proteins have domains that bind in the minor groove as well. Thus, claim 60 defines an inherent characteristic of the zinc finger protein of Cox, III et al. and is therefore anticipated.

#### ***Allowable Subject Matter***

4. Claim 69 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

#### ***Response to Arguments***

5. Applicant's arguments, see page 4 of the response, filed July 8, 2005, with respect to the unavailability of Cox, III et al. as prior art under 35 USC 103(c) have been fully considered and are persuasive. The obviousness rejections of claims 60 and 65 have been withdrawn. Note that claim 65 was previously rejected under 35 USC 102(e) and that rejection is maintained. Claim 60 is now also rejected under 35 USC 102(e), hence, this Office action is a non-final rejection.

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6. Applicants' arguments filed July 8, 2005 have been fully considered but they are not persuasive.

Applicants' arguments are based on a definition of "accessible" that seems to be narrower than that recognized in the art or the specification. The specification defines an accessible region at paragraph 47:

[0047] An **accessible** region is a site in a chromosome, episome or other cellular structure comprising a nucleic acid, in which a target site present in the nucleic acid can be bound by an exogenous molecule which recognizes the target site. *Without wishing to be bound by any particular theory*, it is believed that an accessible region is one that is not packaged into a nucleosomal structure. The distinct structure of an accessible region can often be detected by its sensitivity to chemical and enzymatic probes, for example, nucleases (emphasis added).

From this definition appears that all that is required for DNA to be accessible is the ability to bind an exogenous molecule, there is no requirement that the site cannot be in a nucleosome or that it must contain hypersensitive sites. The belief that "an accessible region is one that is not packaged into a nucleosomal structure" is not a fact, only a belief, not a claim-limiting definition under 35 USC 112, second paragraph. Only claim 65 has a requirement for a hypersensitivity site. Applicants admit at page 3 of the response, "Cox's zinc finger proteins bind to, and regulate expression of a VEGF gene." This is clearly within the scope of the definition of an accessible region in the specification. Applicants' arguments regarding nuclease hypersensitivity appear to be based on an arbitrarily narrow definition of "accessible", and are not found persuasive as applied to the claims that do not require hypersensitivity (all but claim 65). Claim 65

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appears to be an In re Best situation, and it is not clear that the "evidence" provided by the Cirillo and Wong papers applies to the molecules of Cox, III et al. Also, it appears that the molecules of Cox, III et al. definitely bind to hypersensitive sites, as evidenced by Liu et al. (Ref. AF-3 on the IDS filed August 8, 2002). Although this reference is not prior art it may be used to show the inherent properties of what is disclosed in Cox, III et al. Applicants are directed to the paragraph bridging pages 11327 and 11329, which shows that the zinc finger proteins of Cox, III et al. inherently bind to accessible regions of the chromatin. This provides evidence that the "binding sites for Cox's zinc finger proteins **are necessarily and inevitably** present in accessible regions of cellular chromatin," as Applicants state on page 3 of the response to be the test for inherency.

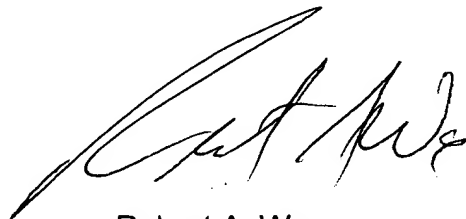
### ***Conclusion***

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Wax whose telephone number is (571) 272-0623. The examiner can normally be reached on Monday through Friday, between 9:00 AM and 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'Robert A. Wax', is positioned above the printed name.

Robert A. Wax  
Primary Examiner  
Art Unit 1653

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